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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/578,507	05/26/2000	Natarajan Ramasubramanyan	2827-4	7987

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EXAMINER	
QIAN, CELINE X	

ART UNIT	PAPER NUMBER
1636	

DATE MAILED: 08/10/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/578,507	RAMASUBRAMANYAN, NATARAJAN	
	Examiner	Art Unit	
	Celine X Qian	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-29,41-51 and 54-64* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-29,41-51 and 54-64* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *26 May 2000* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-29, 41-51 and 54-64 are pending in the application.

This Office Action is in response to the Amendment filed on 5/25/04.

Response to Amendment

The rejection of claims 1-29, 41-51 and 54-64 under 35 U.S.C. 112 2nd paragraph has been withdrawn in light of applicant's amendment of the claims.

The rejection of claims 1-13, 16-29, 41-51 and 54-64 under 35 U.S.C.112 1st paragraph (written description) is maintained for reasons set forth of the record mailed on 2/25/04 and further discussed below.

The rejection of claims 1-29, 41-51 and 54-64 under 35 U.S.C. 112 1st paragraph (scope of enablement) is maintained for reasons set forth of the record mailed on 2/25/04 and further discussed below.

Response to Arguments

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-13, 16-29, 41-51 and 54-64 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

In response to this rejection, Applicant argues that the term "hydrophobic interaction media" and various separation conditions recited in the claims are well recognized by the ordinary skill in the art, and the application is not required to be detailed manual. Applicant further argues that the references cited by Examiner Sandals describes various interaction media and reaction conditions which are indicative of the advanced level of skill in the art. Applicant asserts that the cited Kitamura patent recites "hydrophobic interaction chromatography" and further describes various elution steps as well as other process steps which allow adsorption and desorption from the reaction media. Moreover, Applicant argues that the hydrophobic interaction media comprises a variety of base matrices and hydrophobic ligand, and screening through the commercially available base matrices can be very simple and without undue experimentation. Applicant further argues that the reference titled "Protein Purification" provides a list of commonly used base matrices, and the reference titled "Comparison of chromatography based Q and Membrane based Q" provides the standard procedures for attaching ligands to different spherical and non-spherical matrices. Furthermore, Applicant asserts that the elution of the bound component from a hydrophobic interaction media is achieved by 1) changing the salt concentration; 2) changing the polarity of the solvent; 3) using detergents, and one of ordinary skill in the art may reasonably expect to utilize these or a combination of these to changing hydrophobicity. Moreover, Applicant asserts that pH changes or temperature changes are not used alone to displace the components, and one of ordinary skill in the art can readily determine however the individual and/or combined effects of temperature, pH and salt concentration on the elution pattern from a relatively simple set of experiments. Applicant thus concludes that instant specification has sufficient description to support that

Applicant has possession of the invention at the time the application is filed, and enables the invention more than the exemplified scope.

Applicant's arguments have been fully considered but deemed unpersuasive. Applicant is reminded that the statue requires the specification describes the claimed invention in such a way to convey one skilled in the art that the inventor had possession of the invention at the time the application was filed. Although the specification does not have to be a detailed manual, it needs to describe a representative number of species by their complete structure or by other relevant characteristics. Applicant is also reminded that a patent is a property rather than a precedent, and each patent application is considered individually. Although the Kitamura patent recites "hydrophobic interaction chromatography", it does not necessarily support that written description requirement of the instant application. In addition, Applicant has established that the instant application is filed before the Kitamura patent. As such, this Kitamura patent cannot be solely relied upon to support the written description of the instant application because Applicant has to establish that the written description requirement is satisfied at the time this application is filed. Although the base matrices are commercially available and screening through these matrices can be very simple, the specification still has to describe the structure or characteristics of such hydrophobic interaction media. Assays for screening the matrices is a process rather than the structure or characteristic of such matrices. Moreover, the matrices described in the reference "Protein Purification" is relevant to purification of protein, rather than nucleic acid. The attachment 1 describes the physical property of the intercept Q membrane adsorber, it is unclear how this information" provides the standard procedures for attaching ligands to different spherical and non-spherical matrices as asserted by Applicant. In response to Applicant's

argument with regard to the elution conditions, Applicant is reminded that claims 1-16 explicitly exclude the use of detergent. Moreover, temperature and pH may not be used alone to displace components, the combination of such and/or salt concentration, solvent polarity can also affect hydrophobic interaction. The specification only discloses the change of condition of salt concentration, it fails to describe any other condition. As discussed above, although these conditions may be determined by simple experiments, such experiments do not teach the structural requirements of the claimed invention. As such, the specification fails to describe the invention by its complete structure and other identifying characteristics. Therefore, the written description requirement is not met.

Claims 1-29, 41-51 and 54-64 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method for purifying plasmid DNA from a mixture of same containing at least one host cell impurity comprising: a) forming a solution with said mixture with ammonium sulfate in the range of 2M-4M to allow selective binding of host cell impurity to the hydrophobic interaction media selected from a methcrylate polymer, methacrylate polyethylene glycol copolymer or crosslinked agarose bound to a hydrophobic ligand, contacting said solution with said hydrophobic interaction media, collecting plasmid DNA from said mixture; a method of separating supercoiled plasmid DNA from a mixture of relaxed plasmid DNA and host cell impurity comprising: a) forming a solution with said mixture with 3M ammonium sulfate to allow binding of both plasmid DNA to the hydrophobic interaction media selected from a methcrylate polymer, methacrylate polyethylene glycol copolymer or crosslinked agarose bound to a hydrophobic ligand, b) contacting the solution with

said hydrophobic interaction media, wash/elute the bound DNA with 2.4M ammonium sulfate to remove relaxed plasmid DNA, c) wash/elute the bound DNA with 2.0M ammonium sulfated, d) collect the supercoiled DNA; does not reasonably provide enablement for said methods for using any type of salt at any concentration, or any type of hydrophobic interaction media. Further, the methods are not enabled when other conditions such as pH or temperature are changed for separation of the relaxed or supercoiled DNA. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make/use the invention commensurate in scope with these claims.

In response to this rejection, Applicant argues that the hydrophobic interaction can be effected by a range of salts. Applicant quoted the strength of hydrophobic interaction of the anions and cations from the "Protein Purification" reference, and assert that one skilled in the art can choose with considerable degree of predictability of the salts that will provide necessary hydrophobic interaction. Applicant thus concludes that the specification is enabled for more than the use of ammonium sulfate for the claimed purification process. Applicant further argue that the example in the specification provides evidence that the interaction is not specific to a base matrix or to a specific ligand. Applicant assert that the "Protein Purification" reference provides a variety of commercially available ligands and possible chemistries, possible base matrices that can be used for hydrophobic interaction. Furthermore, Applicant asserts that the hydrophobic interaction strength is the combination of ligand strength and salt strength, each of which can be readily manipulated to achieve certain strength of interaction equivalent to that demonstrated in the examples. Lastly, Applicant argues that there are abundant literature that describes the hydrophobic interaction phenomena, and one of ordinary skill in the art is able to choose from

available hydrophobic interaction media, ligands and salt concentration that will provide similar strengths of interaction as exemplified without undue experimentation. Applicant thus conclude that the claimed invention is enabled to the full scope.

These arguments have been fully considered but deemed unpersuasive. Applicant is reminded that the cited reference, although teaches hydrophobicity of different cations and anion, is primarily directed to the hydrophobic chromatography and protein. The prior art is silent on the interaction between DNA, endotoxin and hydrophobic chromatography, thus the enablement of the instant claims relies primarily on the teaching of the specification. The specification does not teach what degree of hydrophobicity is required for the separation of DNA and endotoxin, or the separation for the relaxed DNA and supercoiled DNA. The specification also fails to teach other conditions such as pH, temperature, and polarity of the solvent that are required for the separation to occur. The specification only provides examples that uses ammonium sulfate at specific concentration for the elution of the DNA, 3 specific base matrices and 3 ligands combination for the DNA purification process. However, the scope of the claim encompasses a purification method wherein any type of hydrophobic interaction media, salt, salt concentration, elution condition can be used. As asserted by Applicant, many factors including temperature, pH, polarity of the solvent, use of detergent, type of salt (anions and cations), ligands and base matrices or a combination of these factors affect hydrophobic interaction. The successful purification of DNA under a specification condition is a result of trial and error rather than routine experimentation. Although there is abundant information regarding to hydrophobic strength in the prior art, the specification still has to teach how to use such information to apply to the claimed purification method and result in the successful purification of the DNA.

However, the specification fails to do that. As such, one of skilled in the art would have to engage in undue experimentation to determine how to use the claimed method when one or more the condition is different from the example given in the specification. Therefore, the claims are not enabled to their full scope.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Celine X Qian whose telephone number is 571-272-0777. The examiner can normally be reached on 9:30-6:00 M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Remy Yucel Ph.D. can be reached on 571-272-0781. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Celine Qian, Ph.D.

Anne-Marie Falk

ANNE-MARIE FALK, PH.D
PRIMARY EXAMINER